# Heat-set gels and egg-like vesicles using two component gel system based on chiral calix[4]arenes†

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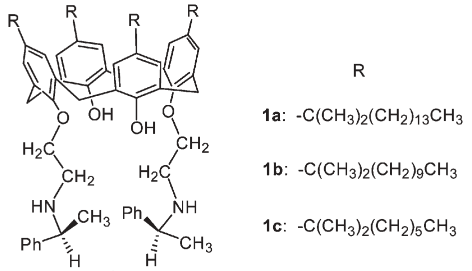
*Received (in Cambridge, UK) 4th September 2007, Accepted 28th September 2007*
*First published as an Advance Article on the web 12th October 2007*
**DOI: 10.1039/b713548c**

**Chiral calix[4]arenes bearing long tertiary alkyl groups at the upper rim and *S*-1-phenylethylamine groups at the lower rim can form heat-set gels and egg-like vesicles enantioselectively with D-2,3-dibenzoyltartaric acid in cyclohexane, which is the first example of heat-set gels resulting from difference in interactions between two component gelators: in addition, the diameter of vesicles decreased with the increase in length of alkyl groups, which could be used to control the size of the vesicles.**

Two-component gel systems, which are significant conceptually different[1a] from their one-component analogues, play an increasingly important role in self-assembling nano- and micro-structures.[1–3] The biggest advantage of two-component gel systems over one-component systems is that the structure and properties of gel nano- and micro-materials can be tuned by changing the molecular ratio of the two components or by changing one of the two components. This has been demonstrated with some typical examples from Smith,[3a] Huc,[3b] and Hong's[3c] groups. However, up to now, nano- and micro-vesicles prepared by two-component gel systems have not been reported, although the vesicles have a specially attractive application in storing, transferring and protecting guest molecules. In fact, even using single component gel systems, the resultant vesicles are also rarely reported.[4]

Gels or viscous fluids induced by heating have great potential applications in many areas, such as medical materials,[5a–c] flow control and separations,[5d] enhanced oil recovery,[5e] thermoresponsive materials,[5f,5g] and food preparation.[5h] However, heat-set gels using a low-molecular-mass gelator (LMMG) are very rare.[5f,5g] After recently finding a novel self-assembly system based on chiral calix[4]arenes,[6] we report that the interaction of chiral calix[4]arene **1**, bearing long tertiary alkyl groups at the upper rim, can, with 2,3-dibenzoyltartaric acid **2** form a heat-set gel, gelatinize cyclohexane through forming vesicles, and by changing the alkyl chain length allow the sizes of the vesicles to be tuned.

Chiral calix[4]arene diamine **1** with long tertiary alkyl groups at the upper rim was synthesized in several steps (Fig. 1). The key step is the introduction of varying lengths of alkyl groups onto the calixarene at the upper rim using a previously reported Friedel–Crafts alkylation[7] but modified to use a long tertiary alkyl alcohol as the reagent and concentrated sulfuric acid as the catalyst. This fulfilled the simplest and shortest route for alkylation of calixarenes at the upper rim. Using $^1$H-NMR spectra, the chiral calix[4]arene diamine **1** is shown to be in the cone conformation, probably due to intramolecular hydrogen bonding between the hydroxyl groups and the ether oxygen atoms at the lower rim.



**1**

**Fig. 1** Schematic structure of calix[4]arene **1**.

A solid mixture of **1a** and L-**2** was prepared beforehand by evaporating a solution of **1a** (5 mM) and L-**2** (10 mM) in chloroform. The mixture was dissolved in cyclohexane by heating and the resultant solution (at the same concentration as that in chloroform) was cooled to 20 °C to give a gel. Performing the same procedure using **1a** and D-**2** under the same conditions led to a clear solution. To our surprise, when heated to 60 °C, the cyclohexane gel of **1a** and L-**2** became a solution, but the cyclohexane solution of **1a** and D-**2** changed into a gel (Fig. 2). The gel that was formed at high temperature was cooled to about 20 °C and after standing for about 5 min the solution regenerated, which was still a solution after standing it at 10 °C for a long time. This process of

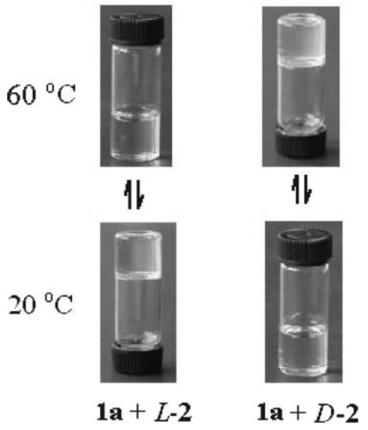


**Fig. 2** Gels changed with temperature.

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† Electronic supplementary information (ESI) available: Experimental materials and methods, spectra and more images. See DOI: 10.1039/b713548c

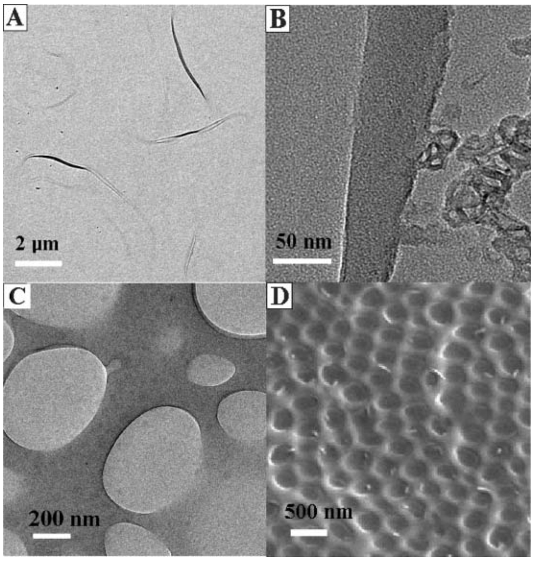

**Fig. 3** (A and B) TEM images of the gel from **1b** and D-**2** at 60 °C. (C) TEM image of solution of **1a** and D-**2** at 20 °C. (D) FE-SEM image of solution of **1a** and D-**2** at 20 °C.

the gel and solution regenerating as the temperature changed could be repeated for many times. In order to avoid mistakes from impurities included accidentally, several batches of **1a** that were prepared at different dates were used and these all gave the same results. After being stored for more than one year at room temperature, **1a** still showed thermally induced gelation.

The gels that resulted from mixture of **1a** and L-**2** at low temperature as well as mixture of **1a** and D-**2** at high temperature were revealed to be fibers by using TEM and FE-SEM (Fig. 3A–B and Fig. S1), but the fibers from the gels of **1a** and D-**2** always existed together with vesicles (Fig. 3B). It is normal that a gel has a structure of nano- or micro-fibers. However, the solution of **1a** and D-**2** at low temperature should also be some kind of aggregate in cyclohexane instead of free molecules or ion pairs. It was sure that the solution was composed of egg-like nano-vesicles, which were shown in both TEM images (Fig. 3C) and FE-SEM images (Fig. 3D).

As shown in Fig. 3B, some small vesicles, which did not transform into fibers at high temperature, existed together with one ribbon-like nanofiber. The shell thickness of the small vesicles was about 5 nm, and the thickness of the up-rolled edges of the ribbon-like nanofiber was also about 5 nm. It indicated that the shell of the small vesicles and the edges of the ribbon-like nanofibers were made of one layer of a **1a**·**2**2·**1a** complex, which has an extended molecular length of about 5 nm, calculated by 3D ChemDraw software. However, at low temperature, the nanofibers as well as the small vesicles are transformed into larger egg-like vesicles with a diameter from about 200 nm to 600 nm as shown in TEM image (Fig. 3C). From this TEM image it was found that the thickness of the vesicles was around 10 nm, indicating that it was composed of two layers of the **1a**·**2**2·**1a** complex. The FE-SEM image in Fig. 3F also showed that the gel of **1a** and D-**2** at low temperature was made of egg-like vesicles that a diameter from 180 nm to 400 nm, which was in accordance with the results obtained from TEM images. In addition, this kind of egg-like vesicle was also confirmed by AFM (Fig. S2†).

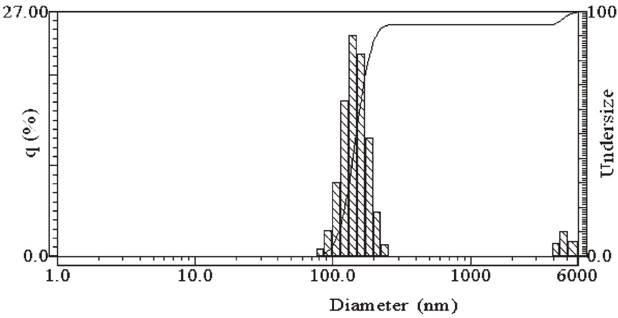

**Fig. 4** Dynamic light scattering (DLS) diagram of solution of **1a** (5 mM) and D-**2** (10 mM) in cyclohexane at 20 °C, the solution was diluted ten times with cyclohexane.

The aggregate behavior of **1a** and D-**2** in solution at low temperature was also investigated by dynamic light scattering (DLS), circular dichroism (CD) spectra and fluorescent spectra, in which the solvent was not evaporated. DLS showed that the solution of **1a** and D-**2** at 20 °C included mainly small particles (94%) with diameters in the range of 90–250 nm, which were accordant to the above results obtained by microscopy. However, larger aggregates (6%) with diameters in the range of 4–6 μm were also observed (Fig. 4). This confirmed that two kinds of aggregates coexist in the solution of **1a** and D-**2** in cyclohexane at 20 °C, the main ones being vesicles and the minor ones being nanofibers. This was not surprising because the nanofibers and nanovesicles can be transformed into each other but the vesicles are more stable at low temperatures. The circular dichroism (CD) spectra from mixing of **1a** and D-**2** at 60 °C and 20 °C were completely different (Fig. S3†). The gel diluted 6 times with cyclohexane at 60 °C showed positive Cotton effects at 247, 236, 227 and 220 nm, but the diluted solution at the same times and solvent at 20 °C showed negative Cotton effects at 239 nm and 224 nm. This confirmed that the aggregates formed at high temperature and low temperature were totally different. We also explored the aggregate behavior with a fluorescent probe, PEB, a very kind of stable coumarine (Fig. S4†). The intensity of emission band of PEB at 427 nm in solution of **1a** and D-**2** was always larger than that in pure cyclohexane at 20 °C. It is known that a fluorescent probe will exhibit a more intense fluorescence upon binding to a supramolecular surface due to the decrease of self-quenching.[8] This indicated that the solution of **1a** and D-**2** at low temperatures did truly include aggregates although the solution seemed to be clear and not very viscous.

Compared with **1a**, both **1b** and **1c** could gelatinize cyclohexane at 20 °C together with either L-**2** or D-**2** under the same conditions, and the resultant gels had a similar tendency to change with temperature. Upon heated from 20 °C to 60 °C, the gel resulting from a mixture of **1b** or **1c** and L-**2** became a solution, but the gel from a mixture of **1b** or **1c** and D-**2** did not melt and remained the same. Standing at 10 °C for more than one hour, the gel of **1b** or **1c** and L-**2** remained a gel, and the gel of **1b** or **1c** and D-**2** became a suspension. Moreover, all gels obtained from **1b** and **1c** were revealed to contain vesicles, as shown in TEM images (Fig. 5 and Fig. S11–13†). The diameter of the vesicles ranged from 400 nm to 1.0 μm for **1b** (Fig. 5B)and from 1.0 μm to 2.5 μm for **1c** (Fig. 5C), compared to a diameter of 200 nm to 600 nm for **1a** vesicles (Fig. 5A and Fig. 3C–D). This means that the diameter of the vesicles decreased with an increase in the length of the alkyl groups, so

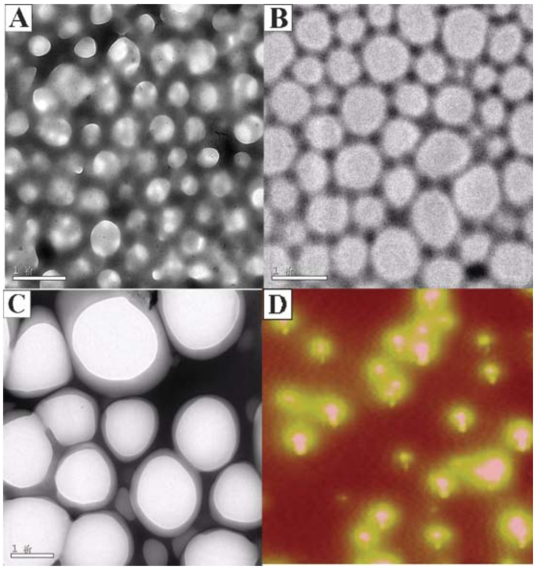

**Fig. 5** (A, B and C) TEM images of gel from (A) **1a** and D-**2**, (B) **1b** and D-**2**, (C) **1c** and D-**2** (scale bar for A, B and C, 1 μm). (D) AFM images of gel from **1b** and D-**2** on freshly broken mica (25 × 25 μm).

that the size of vesicles could be controled by changing the length of the alkyl groups at the upper rim of the calix[4]arene. This result is consistent with Jiang *et al.*'s report in which they found that the size of the vesicles based on amphiphilic calixarenes decreased with the increasing length of the hydrophilic chains.[9] The structure of the vesicles resulting from a mixture of **1b** and D-**2** was confirmed by AFM images (Fig. 5D) and FE-SEM images (Fig. S9–10†). AFM imaging showed that the aggregates were spherical entities with sizes ranging from 1.0 μm to 2.0 μm, which was similar to the result observed with the TEM images. Probably due to the bigger size and reduced solubility (shorter alkyl chain) of the vesicles from **1b** and **1c** compared to **1a**, the mixture of **1b** or **1c** and D-**2** is a gel but that of **1a** and D-**2** is a solution at room temperature.

In general, with long alkyl group(s), an amphiphile is more prone to self-assembly due to hydrophobicity and van der Waals attraction between the long alkyl groups. Therefore not only the mixture of **1a** and L-**2** but also that of **1a** and D-**2** can self-assemble into nanofibers. However, the fibrous assembles of **1a**–D-**2** are not stable due to the unmatched interaction between the chiral centers of **1a** and D-**2**. The unmatched interaction will increase as the temperature decreases and the intermolecular distance shortens. By curving the flat lamellar, the repulsion between the chiral centers of **1a** and D-**2** can be reduced, so that fibrous objects spontaneously transform into vesicles. This is similar to lamellar gels and spontaneous vesicles in catanionic surfactant mixtures.[10] **1b** and **1c** bear slightly shorter alkyl groups and can only form vesicles because the van der Waals attraction between alkyl groups decreases and the unmatched interaction of chiral centers of **1** and D-**2** stand out much more. At lower temperatures the vesicle gel will become more a stable suspension and even precipitate.

In conclusion, for the first time we have demonstrated that heat-set gels can form through the transformation from vesicles to nanofibers due to a difference in interaction between two component chiral gelators. This finding provides a new approach to heat-set gels, which have potential applications for thermo-responsive materials.

The authors thank National Natural Science Foundation of China for financial support (No. 20072007 and 20672039) and thank the Analytical and Testing Centre at Huazhong University of Science and Technology for measurement.

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